REMARKS

Claims 1-38 are pending in the present application.

Objections to the specification

The Examiner objects to the specification for the noted typographical error on page 4, line 11. The specification has been amended to correct the indicated error. Withdrawal of the objection is respectfully requested.

Objections to the claims

Claim 4 has been objected to for recitation of "a solid phase having binding sites." Claim 4 has been amended as suggested by the Examiner to recite "having binding sites incorporated thereon."

Claim 10 has been objected to as being a duplicate of claim 8. Claim 8 was incorrectly replicated in the Preliminary Amendment of October 10, 2001. This typographical error has been corrected.

Rejections under 35 U.S.C. §112, second paragraph

The claims have been rejected under 35 U.S.C. §112, second paragraph as being unclear for the reasons detailed on pages 3-6 of the Office Action. The claims have been amended as indicated on the attached "marked-up" version to address these issues. No new matter has been added with the amendments. In addition, the

following remarks are submitted to address any rejections that were not addressed through amendment.

a) Several of the claims have been rejected with the assertion that there is no antecedent basis for "the ratio." Applicants traverse these rejections and withdrawal thereof is respectfully requested. "Inherent components of elements recited have antecedent basis in the recitation of the components themselves. For example, the limitation "the outer surface of said sphere" would not require an antecedent recitation that the sphere has an outer surface." M.P.E.P. §2173.05(e). The present claims recite two elements. As such, the "ratio" of the amounts of the elements is an inherent feature and the claims would make no sense if amended to recite "a ratio" rather than "the ratio."

b) Claim 38 has been rejected as being vague in the recitation of "no more than about 1:20." It appears from the Office Action that the Examiner believes that some units should be recited. However, the recitation in claim 38 of "1:20" is a ratio, and therefore, no units should be recited. Withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C.§102(b)

Claims 1, 4, 6-8, 10, 13, 14, 15, 22, 25 and 28 have been rejected under 35 U.S.C. §102(b) as being anticipated by either EP

0105714 (hereinafter referred to as "EP '714"). Claims 1-3, 8-10, 13, 14, 16 and 17 have been rejected under 35 U.S.C. §102(b) as being anticipated by US 6,184,042 (hereinafter referred to as U.S. '042"). Both EP '714 and U.S. '042 are asserted to teach sandwich assays wherein an excess amount of receptor to analyte is used.

Applicants traverse these rejections and withdrawal thereof is respectfully requested. "To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either explicitly or inherently." In re Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1431 (Fed. Cir. 1997).

The present invention, as encompassed by claim 1, is drawn to a method of determining an analyte in a sample comprising the steps of:

a) contacting the sample with an amount of a receptor which binds specifically to the analyte to form an analyte/receptor complex, and which is in excess of that required to bind all analyte in the sample,

b) isolating on a solid phase a specified fraction of receptor contacted with the analyte, including analyte/receptor complex and unreacted receptor,

c) detecting the amount of analyte/receptor complex in said isolated specified fraction, and

d) from the detected amount of analyte/receptor complex, determining the concentration of analyte in the sample.

As note by the Examiner both the present invention and the assays of EP '714 and U.S. '042 are sandwich assays using an excess of receptor to analyte. However, the presently claimed invention differs from the sandwich assays of EP '714 and U.S. '042 in several ways. 1) The assays of the references use a mixture of solid phase bound and free receptor, whereas the present invention uses only one receptor type. See, for example, column 2, lines 26-31 of U.S. '042. 2) Claim 1 further recites the sequential binding of affinity reagents, as indicated recitation of "steps" a) and b). The assays of the references, on the other hand, "one-step" assays. 3) Finally, as recited in step b) of claim 1, the present invention isolates a specified fraction of the receptor, with or without bound analyte. As such, the present invention is distinguished from the assays of EP '714 and U.S. '042 and withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. §103

Claims 11 and 12 have been rejected under 35 U.S.C. §103 as being obvious over U.S. '042 combined with U.S. Pat. No. 6,319,676 (hereinafter referred to as "U.S. '676"). U.S. '676 is asserted to

teach a lateral flow matrix using a sandwich technique in which receptors are immobilized in the reaction zone of the flow matrix.

Claim 18 has been rejected under 35 U.S.C. §103 as being obvious over U.S. '042 combined with U.S. Pat. No. 6,316,205 (hereinafter referred to as "U.S. '205"). U.S. '205 is asserted to teach a sandwich assay in which the sample is whole blood.

Claims 19-28 and 33-38 have been rejected under 35 U.S.C. §103 as being obvious over U.S. '042 and U.S. '676 combined with U.S. Pat. No. 5,420,016 (hereinafter referred to as "U.S. '016"). U.S. '016 is asserted to teach the assembly of components into a test kit.

Applicants traverse these rejections and withdrawal thereof is respectfully requested. As discussed above, the present invention is distinguished from the primary references in the features of 1) using only one receptor type; 2) the sequential binding of affinity reagents; and 3) the isolation a specified fraction of the receptor, with or without bound analyte.

There is no disclosure in any of the secondary references of these three features of the present invention. As such, combining the secondary references of U.S. '676, U.S. '205 or U.S. '016 with the teachings of the primary references will not achieve the invention. In addition, the present invention has the advantageous property of improved results with lateral flow assays on high

concentration samples. As such, the present invention is not obvious over the cited prior art references and withdrawal of the rejections is respectfully requested.

A marked-up version of the claims showing all changes is attached hereto.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong, Ph.D. (Reg. 40,069) at the telephone number of the undersigned below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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MARKED-UP VERSION SHOWING CHANGES

IN THE SPECIFICATION

Please replace the paragraph beginning at page 4, line 9 has been amended as follows.

--The term "amount" as used herein usually means binding capacity. Thus, for example, when it is stated that the amount of analyte-specific receptor is in excess of the amount of analyte, it means that there is more analyte-specific receptor than necessary to bind all analyte. Usually, there is a 1:1 reaction **ratio** ~~ration~~ between e.g. the analyte and the analyte-specific receptor, or between the analyte specific receptor and the immobilized receptor-binding ligand. In such a case, the binding capacities of the respective species correspond to their molar amounts. Other reaction ratios are, however, also possible. For example, the immobilized ligand may be capable of binding more than one analyte-specific receptor.--

IN THE CLAIMS

Claims 1-2, 4-8, 11, 16, 19-26, 29-30, and 32-38 have been amended as follows:

1. (Twice Amended) A method of determining an analyte in a sample comprising the steps of:

a) contacting the sample with ~~a specified~~ **an** amount of a receptor which binds specifically to the analyte to form an analyte/receptor complex, ~~said specified amount of receptor being~~ **and which is** in excess of that required to bind all analyte in the sample,

b) isolating on a solid phase a specified fraction of ~~the amount of~~ receptor contacted with the analyte, including analyte/receptor complex and unreacted receptor,

c) detecting the amount of analyte/receptor complex in said isolated specified fraction, and

d) from the detected amount of analyte/receptor complex, determining the concentration of analyte in the sample.

2. (Amended) The method according to claim 1 in which the sample has a ~~high~~ concentration **of greater than 1 nmole/litre**.

4. (Twice Amended) The method according to claim 1 or 2, wherein isolating said specified fraction of ~~the amount of~~ receptor contacted with the sample on the solid phase comprises providing a solid phase having binding sites **incorporated thereon** for the receptor, and after contacting the sample, or an aliquot thereof, with a liquid phase containing the receptor, binding said specified fraction of receptor to the solid phase.

5. (Amended) The method according to claim 4, wherein ~~the whole amount of~~ **all of the** receptor **contacted with the sample** has reactivity towards said binding sites on the solid phase, and ~~the~~ receptor-binding capacity of the solid phase is less than ~~the~~ solid-phase binding capacity of receptor contacted with the sample.

6. (Amended) The method according to claim 4, wherein only a specified fraction ~~of the amount~~ of receptor contacted with the sample has reactivity towards said binding sites on the solid phase.

7. (Twice Amended) The method according to claim 1 or 2, wherein isolating said specified fraction of ~~the amount of~~ receptor on the solid phase comprises contacting the sample with a specified amount of receptor, a specified fraction of which amount is immobilized to said solid phase and the remaining amount of receptor being in a liquid phase.

8. (Twice Amended) The method according to claim 1, wherein **the receptor comprises a first part that binds specifically to the analyte, and a second part that binds to the solid phase** ~~in step c)~~

~~the analyte/receptor complex is detected by a labeled detection reagent which binds specifically to the analyte~~.

11. (Twice Amended) The method according to claim 1, wherein the ratio between said isolated fraction of ~~the amount of active analyte binding~~ receptor and ~~the total amount of active analyte-binding~~ receptor contacted with the sample is in ~~the~~ **a** range of from about 1:2 to about 1:1000.

16. (Twice Amended) The method according to claim **9** ~~7~~, wherein the specific binding pair is biotin-avidin or biotin-strepavidin.

19. (Amended) A test kit for determining an analyte in a sample, comprising a specified amount of a receptor ~~substance~~ **reagent** having a first part which binds specifically to the analyte, and a solid phase member having immobilized thereon a ligand which binds specifically to a second part of the receptor, **wherein** ~~the~~ receptor-binding capacity of said ligand **immobilized** on the solid phase member ~~being~~ **is** less than ~~the~~ ligand-binding capacity of said specified amount of receptor **reagent** ~~substance~~.

20. (Twice Amended) The test kit according to claim 19, wherein the ratio between ~~the~~ receptor-binding capacity of ligand

immobilized on the solid phase and ~~the~~ ligand-binding capacity of the analyte-specific receptor **reagent** ~~substance~~ is in the range of from about 1:2 to about 1:1000.

21. (Twice Amended) The test kit according to claim 19 or 20, further comprising a lateral flow membrane strip having said receptor-binding ligand immobilized in or on a reaction zone of the membrane and having said analyte-binding receptor **reagent** ~~substance~~ dissolvably pre-deposited in or on the membrane upstream of the reaction zone.

22. (Amended) A test kit for determining an analyte in a sample, comprising a specified amount of a receptor ~~substance~~ **reagent** having a first part which binds specifically to the analyte, **wherein** only a specified fraction of ~~the amount of~~ receptor ~~substance having~~ **reagent has** a second part ~~capable of binding~~ **which binds** to a specific ligand, and a solid phase member having said specific ligand immobilized thereon.

23. (Twice Amended) The test kit according to claim 22, wherein the ratio between ~~the amount of~~ ligand-binding analyte-specific receptor and ~~the total amount of~~ analyte-specific receptor is in ~~the~~ **a** range of from about 1:2 to about 1:1000.

24. (Twice Amended) The test kit according to claim 22 or 23, further comprising a lateral flow membrane strip having said receptor-binding ligand immobilized in or on a reaction zone of the membrane and having said analyte-binding receptor ~~substance~~ **reagent** dissolvably pre-deposited in or on the membrane upstream of the reaction zone.

25. (Amended) A test kit for determining an analyte in a sample, comprising a first specified amount of an analyte-binding receptor **reagent** ~~substance~~, and a solid phase member having immobilized thereon a second specified amount of said analyte-binding receptor ~~substance~~ **reagent**.

26. (Twice Amended) The test kit according to claim 25, wherein the ratio between said second amount of analyte-binding receptor ~~substance~~ **reagent** immobilized to the solid phase, and ~~the sum of~~ said first and second amounts of analyte-binding receptor **reagent together** ~~substance~~ is in ~~the~~ range of from about 1:2 to about 1:1000.

29. (Amended) The method according to claim 9, wherein the ratio between said isolated fraction of ~~the amount of active~~

analyte-binding receptor and ~~the total amount of active~~ analyte-binding receptor contacted with the sample is in the range of from about 1:5 to 1:100.

30. (Amended) The method according to claim 9, wherein the ratio between said isolated fraction of ~~the amount of active~~ analyte-binding receptor and ~~the total amount of active~~ analyte-binding receptor contacted with the sample is no more than about 1:20.

32. (Amended) The method according to claim **31** ~~29~~, wherein said lateral flow matrix is a membrane strip.

33. (Amended) The test kit according to claim 20, wherein the ratio between the receptor-binding capacity of ligand immobilized on the solid phase and the ligand-binding capacity of the analyte-specific receptor ~~substance~~ **reagent** is in the range of from about 1:5 to 1:100.

34. (Amended) The test kit according to claim 20, wherein the ratio between the receptor-binding capacity of ligand immobilized on the solid phase and the ligand-binding capacity of the analyte-specific receptor ~~substance~~ **reagent** is no more than about 1:20.

35. (Amended) The test kit according to claim 23, wherein the ratio between ~~the amount of~~ ligand-binding analyte-specific receptor and ~~the total amount of~~ analyte-specific receptor is in the range of from about 1:5 to 1:100.

36. (Amended) The test kit according to claim 23, wherein the ratio between ~~the amount of~~ ligand-binding analyte-specific receptor and ~~the total amount of~~ analyte-specific receptor is no more than about 1:20.

37. (Amended) The test kit according to claim 26, wherein the ratio between said second amount of analyte-binding receptor substance immobilized to the solid phase, and ~~the sum of~~ said first and second amounts of analyte-binding receptor ~~substance~~ **reagent together** is in the range of from about 1:5 to 1:100.

38. (Amended) The test kit according to claim 26, wherein the ratio between said second amount of analyte-binding receptor substance immobilized to the solid phase, and ~~the sum of~~ said first and second amounts of analyte-binding receptor ~~substance~~ **reagent together** is no more than about 1:20.--